

	Type	L #	Hits	Search Text	Dbs	Time Stamp	Comments	Error Definition	Errors
1	BRS	L1	69	phospholamban	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:53			0
2	BRS	L2	27	1 same (inactivat\$3 or deactivat\$3 or inhibit\$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:54			0
3	BRS	L4	9433	(molecular adj model\$3) or (computer adj model\$3)	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:56			0
4	BRS	L5	0	2 same 4	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:56			0
5	BRS	L6	0	(ligand adj binding) same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:57			0
6	BRS	L7	0	(cytosolic adj domain) same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:58			0
7	BRS	L8	2	caAltPase	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:58			0
8	BRS	L9	28	ca-ATPase	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:58			0
9	BRS	L10	1	(8 or 9) same 1	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/0 4 10:59			0

	Type	L #	Hits	Search Text	Dbs	Time Stamp	Comments	Error Definition	Error
10	BRS	L11	54	miller adj allan.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/04 10:59			0
11	BRS	L12	39	treco adj douglas.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/04 11:00			0
12	BRS	L13	39	selden adj richard.in.	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/04 11:00			0
13	BRS	L14	0	(11 or 12 or 13) and 2	USPAT; US-PGPUB; EPO; JPO; DERWENT	2003/03/04 11:01			0

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=> file medline caplus biosis embase scisearch agricola

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FILE 'AGRICOLA' ENTERED AT 11:04:46 ON 04 MAR 2003

=> s phospholamban

L1 5599 PHOSPHOLAMBAN

=> s l1 (p) (inactivat? or deactivat? or inhibit?)

L2 1495 L1 (P) (INACTIVAT? OR DEACTIVAT? OR INHIBIT?)

=> s (molecul? model?) or (computer model?)

5 FILES SEARCHED...

L3 113184 (MOLECUL? MODEL?) OR (COMPUTER MODEL?)

=> s l2 (p) l3

L4 14 L2 (P) L3

=> duplicate remove l4

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'

KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n

PROCESSING COMPLETED FOR L4

L5 4 DUPLICATE REMOVE L4 (10 DUPLICATES REMOVED)

=> d l5 1-4 ibib abs

L5 ANSWER 1 OF 4

MEDLINE

DUPLICATE 1

ACCESSION NUMBER: 2001553881 MEDLINE

DOCUMENT NUMBER: 21486400 PubMed ID: 11477077

TITLE: Role of cysteine residues in structural stability and function of a transmembrane helix bundle.

AUTHOR: Karim C B; Paterlini M G; Reddy L G; Hunter G W; Barany G; Thomas D D

CORPORATE SOURCE: Departments of Biochemistry, Molecular Biology, and Biophysics, Medicinal Chemistry, University of Minnesota, Minneapolis, Minnesota 55455, USA.. cbk@ddt.biochem.umn.edu

CONTRACT NUMBER: 1K02 HL04209 (NHLBI)

DA0037 (NIDA)

GM27906 (NIGMS)

GM51628 (NIGMS)

SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (2001 Oct 19) 276 (42) 38814-9.

Journal code: 2985121R. ISSN: 0021-9258.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200112

ENTRY DATE: Entered STN: 20011016

Last Updated on STN: 20030105

AB To study the structural and functional roles of the cysteine residues at positions 36, 41, and 46 in the transmembrane domain of \*\*\*phospholamban\*\*\* (PLB), we have used Fmoc (N-(9-fluorenyl)methoxycarbonyl) solid-phase peptide synthesis to prepare alpha-amino-n-butyric acid (Abu)-PLB, the analogue in which all three cysteine residues are replaced by Abu. Whereas previous studies have shown that replacement of the three Cys residues by Ala (producing Ala-PLB) greatly destabilizes the pentameric structure, we hypothesized that replacement of Cys with Abu, which is isosteric to Cys, might preserve the pentameric stability. Therefore, we compared the oligomeric structure (from SDS-polyacrylamide gel electrophoresis) and function (\*\*\*inhibition\*\*\* of the Ca-ATPase in reconstituted membranes) of Abu-PLB with those of synthetic wild-type PLB and Ala-PLB. \*\*\*Molecular\*\*\* modeling provides structural and energetic insight into the different oligomeric stabilities of these molecules. We conclude that 1) the Cys residues of PLB are not necessary for pentamer formation or \*\*\*inhibitory\*\*\* function; 2) the steric properties of cysteine residues in the PLB transmembrane domain contribute substantially to pentameric stability, whereas the polar or chemical properties of the sulfhydryl group play only a minor role; 3) the functional potency of these PLB variants does not correlate with oligomeric stability; and 4) acetylation of the N-terminal methionine has neither a functional nor a structural effect in full-length PLB.

L5 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER: 2001:34634 CAPLUS

DOCUMENT NUMBER: 134:218589

TITLE: Reexamination of the role of the leucine/isoleucine zipper residues of phospholamban in inhibition of the Ca<sup>2+</sup> pump of cardiac sarcoplasmic reticulum

AUTHOR(S): Cornea, Razvan L.; Autry, Joseph M.; Chen, Zhenhui; Jones, Larry R.

CORPORATE SOURCE: Department of Medicine and the Krannert Institute of Cardiology, Indiana University School of Medicine, Indianapolis, IN, 46202, USA

SOURCE: Journal of Biological Chemistry (2000), 275(52), 41487-41494

CODEN: JBCHA3; ISSN: 0021-9258

PUBLISHER: American Society for Biochemistry and Molecular Biology

DOCUMENT TYPE: Journal

LANGUAGE: English

AB Phospholamban is a small phosphoprotein inhibitor of the Ca<sup>2+</sup>-pump in cardiac sarcoplasmic reticulum, which shows a distinct oligomeric distribution between monomers and homopentamers that are stabilized through Leu/Ile zipper interactions. A two-faced model of phospholamban inhibition of the Ca<sup>2+</sup>-pump was proposed, in which the Leu/Ile zipper residues located on one face of the transmembrane .alpha.-helix regulate the pentamer to monomer equil., whereas residues on the other face of the helix bind to and inhibit the pump. Here we tested this two-faced model of phospholamban action by analyzing the functional effects of a new series of Leu/Ile zipper mutants. Pentameric stabilities of the mutants were quantified at different SDS concns. We show that several phospholamban mutants with hydrophobic amino acid substitutions at the Leu/Ile zipper region retain the ability to form pentamers but at the same time give the same or even stronger (i.e. L37I-PLB) inhibition of the Ca<sup>2+</sup>-pump than do mutants that are more completely monomeric. Steric constraints prevent the Leu/Ile zipper residues sequestered in the interior of the phospholamban pentamer from binding to the Ca<sup>2+</sup>-pump, leading to the conclusion that the zipper residues access the pump from the phospholamban monomer, which is the active inhibitory species. A modified model of phospholamban transmembrane domain action is proposed, in which the membrane span of the phospholamban monomer maintains contacts with the Ca<sup>2+</sup>-pump around most of its circumference, including residues located in the Leu/Ile zipper region.

REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L5 ANSWER 3 OF 4 MEDLINE

ACCESSION NUMBER: 2000071613 MEDLINE

DOCUMENT NUMBER: 20071613 PubMed ID: 10603946

DUPLICATE 2

TITLE: Direct spectroscopic detection of molecular dynamics and interactions of the calcium pump and phospholamban

AUTHOR: Thomas D D; Reddy L G; Karim C B; Li M; Cornea R; Autry J M; Jones L R; Stamm J

CORPORATE SOURCE: Department of Biochemistry, University of Minnesota Medical School, Minneapolis 55455, USA.. ddt@ddt.biochem.umn.edu

CONTRACT NUMBER: GM27906 (NIGMS)  
HL06308 (NHLBI)  
HL49428 (NHLBI)

SOURCE: ANNALS OF THE NEW YORK ACADEMY OF SCIENCES, (1998 Sep 16)  
853 186-94. Ref: 23  
Journal code: 7506858. ISSN: 0077-8923.

PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
General Review; (REVIEW)  
(REVIEW, TUTORIAL)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 200001

ENTRY DATE: Entered STN: 20000124  
Last Updated on STN: 20000124  
Entered Medline: 20000107

AB In order to test \*\*\*molecular\*\*\* \*\*\*models\*\*\* of cardiac calcium transport regulation, we have used spectroscopy to probe the structures, dynamics, and interactions of the Ca pump (Ca-ATPase) and \*\*\*phospholamban\*\*\* (PLB) in cardiac sarcoplasmic reticulum (SR) and in reconstituted membranes. Electron paramagnetic resonance (EPR) and phosphorescence of probes bound to the Ca pump show that the activity of the pump is quite sensitive to its oligomeric interactions. In cardiac SR, PLB aggregates and \*\*\*inhibits\*\*\* the pump, and both effects are reversed by PLB phosphorylation. Previous analyses of PLB's oligomeric state were only in detergent solutions, so we used EPR and fluorescence to determine the oligomeric structure of PLB in its native state in lipid bilayers. Wild-type PLB is primarily oligomeric in the membrane, while the mutant L37A-PLB is monomeric. For both proteins, phosphorylation shifts the dynamic monomer-oligomer equilibrium toward oligomers, and induces a similar structural change, as indicated by tyrosine fluorescence; yet L37A-PLB is more effective than wild-type PLB in \*\*\*inhibiting\*\*\* and aggregating the pump. Fluorescence energy transfer shows that the Ca pump preferentially binds monomeric PLB. These results support a reciprocal aggregation model for Ca pump regulation, in which the Ca pump is aggregated and \*\*\*inhibited\*\*\* by association with PLB monomers, and phosphorylation of PLB reverses these effects while decreasing the concentration of PLB monomers. To investigate the structure of the PLB pentamer in more detail, we measured the reactivities of cysteine residues in the transmembrane domain of PLB, and recorded EPR spectra of spin labels attached to these sites. These results support an atomic structural model, based on molecular dynamics simulations and mutagenesis studies, in which the PLB pentamer is stabilized by a leucine-isoleucine zipper within the transmembrane domain.

L5 ANSWER 4 OF 4 MEDLINE DUPLICATE 3

ACCESSION NUMBER: 95271668 MEDLINE

DOCUMENT NUMBER: 95271668 PubMed ID: 7752243

TITLE: Structural model of the phospholamban ion channel complex in phospholipid membranes.

AUTHOR: Arkin I T; Rothman M; Ludlam C F; Aimoto S; Engelman D M; Rothschild K J; Smith S O

CORPORATE SOURCE: Department of Cell Biology, Yale University School of Medicine, New Haven, CT 06510, USA.

CONTRACT NUMBER: GM 22778 (NIGMS)  
GM 46732 (NIGMS)  
GM 47527 (NIGMS)

SOURCE: JOURNAL OF MOLECULAR BIOLOGY, (1995 May 12) 248 (4) 824-34.  
Journal code: 2985088R. ISSN: 0022-2836.

PUB. COUNTRY: ENGLAND: United Kingdom

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)

LANGUAGE: English

FILE SEGMENT: Priority Journals

ENTRY MONTH: 199506

ENTRY DATE: Entered STN: 19950629

AB \*\*\*Phospholamban\*\*\* is a 52 amino acid residue membrane protein involved with the regulation of calcium levels across sarcoplasmic reticulum membranes in cardiac muscle cells. The N-terminal 30 amino acid residues of the protein are largely hydrophilic and include two sites whose phosphorylation is thought to dissociate an \*\*\*inhibitory\*\*\* complex between \*\*\*phospholamban\*\*\* and  $\text{Ca}^{2+}$  ATPase. The C-terminal 22 amino acid residues are largely hydrophobic, anchor the protein in the membrane and are responsible for  $\text{Ca}^{2+}$  selective ion conductance. Specific interactions between the transmembrane domains stabilize a pentameric protein complex. We have obtained circular dichroism (CD), transmission Fourier transform infrared (FTIR) and attenuated total reflection Fourier transform infrared (ATR-FTIR) spectra of the full-length protein and have compared these results to those from a 28 residue peptide that includes the transmembrane domain. Both proteins reconstituted into phospholipid membranes are largely alpha-helical by CD and FTIR. Polarized ATR-FTIR measurements show that both the cytosolic and transmembrane helices are oriented perpendicular to the membrane plane with a tilt of  $28 (+/- 6)$  degrees with respect to the membrane normal. This tilt angle is in close agreement to that calculated from a model for the transmembrane domain of \*\*\*phospholamban\*\*\* suggested by mutagenesis and \*\*\*molecular\*\*\* modeling. Phosphorylation does not significantly change the secondary structure or orientation of the protein. The pentameric complex is modeled as a left-handed coiled-coil of five long helices (40 (+/- 3) residues) that extend across the membrane from the luminal carboxy terminus to the phosphorylation site in the cytoplasm. The helix bundle forms a perpendicular ion pore that may begin at a distance (17 to 29 Å) from the membrane surface. Based on the above, we propose a mechanism by which \*\*\*phospholamban\*\*\* regulates  $\text{Ca}^{2+}$  levels across membranes that takes into account both its selective ion conductance and \*\*\*inhibitory\*\*\* association with the  $\text{Ca}^{2+}$  pump.

=> d his

(FILE 'HOME' ENTERED AT 11:04:23 ON 04 MAR 2003)

FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT 11:04:46 ON 04 MAR 2003

L1 5599 S PHOSPHOLAMBAN  
 L2 1495 S L1 (P) (INACTIVAT? OR DEACTIVAT? OR INHIBIT?)  
 L3 113184 S (MOLEкул? MODEL?) OR (COMPUTER MODEL?)  
 L4 14 S L2 (P) L3  
 L5 4 DUPLICATE REMOVE L4 (10 DUPLICATES REMOVED)

=> s cyclic peptide

L6 10886 CYCLIC PEPTIDE

=> s l2 (p) l6

L7 0 L2 (P) L6

=> s ca-ATPase

L8 5430 CA-ATPASE

=> s l8 (p) l2

L9 107 L8 (P) L2

=> s l9 (p) Model?

L10 19 L9 (P) MODEL?

=> duplicate remove l10

DUPLICATE PREFERENCE IS 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH'  
 KEEP DUPLICATES FROM MORE THAN ONE FILE? Y/(N):n  
 PROCESSING COMPLETED FOR L10

L11 5 DUPLICATE REMOVE L10 (14 DUPLICATES REMOVED)

=> s l11 not l5

L12 3 L11 NOT L5

=> d l12 1-3 ibib abs

L12 ANSWER 1 OF 3 MEDLINE  
 ACCESSION NUMBER: 1999343544 MEDLINE  
 DOCUMENT NUMBER: 99343544 PubMed ID: 10413504  
 TITLE: Different anesthetic sensitivities of skeletal and cardiac isoforms of the Ca-ATPase.  
 AUTHOR: Karon B S; Autry J M; Shi Y; Garnett C E; Inesi G; Jones L R; Kutchai H; Thomas D D  
 CORPORATE SOURCE: Department of Biochemistry, University of Minnesota Medical School, Minneapolis 55455, USA.  
 CONTRACT NUMBER: GM27906 (NIGMS)  
 GM50764 (NIGMS)  
 HL49428 (NHLBI)

+  
 SOURCE: BIOCHEMISTRY, (1999 Jul 20) 38 (29) 9301-7.  
 Journal code: 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199909  
 ENTRY DATE: Entered STN: 19990925  
 Last Updated on STN: 19990925  
 Entered Medline: 19990915

AB We have previously shown that low levels of the volatile anesthetic halothane activate the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* in skeletal sarcoplasmic reticulum (SR), but \*\*\*inhibit\*\*\* the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* in cardiac SR. In this study, we ask whether the differential \*\*\*inhibition\*\*\* is due to (a) the presence of the regulatory protein \*\*\*phospholamban\*\*\* in cardiac SR, (b) different lipid environments in skeletal and cardiac SR, or (c) the different \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* isoforms present in the two tissues. By expressing skeletal (SERCA 1) and cardiac (SERCA 2a) isoforms of the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* in Sf21 insect cell organelles, we found that differential anesthetic effects in skeletal and cardiac SR are due to differential sensitivities of the SERCA 1 and SERCA 2a isoforms to anesthetics. Low levels of halothane \*\*\*inhibit\*\*\* the SERCA 2a isoform of the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\*, and have little effect on the SERCA 1 isoform. The biochemical mechanism of halothane \*\*\*inhibition\*\*\* involves stabilization of E2 conformations of the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\*, suggesting direct anesthetic interaction with the ATPase. This study establishes a biochemical \*\*\*model\*\*\* for the mechanism of action of an anesthetic on a membrane protein, and should lead to the identification of anesthetic binding sites on the SERCA 1 and SERCA 2a isoforms of the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\*.

L12 ANSWER 2 OF 3 MEDLINE  
 ACCESSION NUMBER: 1998263185 MEDLINE  
 DOCUMENT NUMBER: 98263185 PubMed ID: 9601048  
 TITLE: Phosphorylation-induced structural change in phospholamban and its mutants, detected by intrinsic fluorescence.  
 AUTHOR: Li M; Cornea R L; Autry J M; Jones L R; Thomas D D  
 CORPORATE SOURCE: Department of Biochemistry, University of Minnesota Medical School, Minneapolis 55455, USA.  
 CONTRACT NUMBER: GM27906 (NIGMS)  
 HL06308 (NHLBI)  
 HL49428 (NHLBI)

SOURCE: BIOCHEMISTRY, (1998 May 26) 37 (21) 7869-77.  
 Journal code: 0370623. ISSN: 0006-2960.  
 PUB. COUNTRY: United States  
 DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)  
 LANGUAGE: English  
 FILE SEGMENT: Priority Journals  
 ENTRY MONTH: 199806  
 ENTRY DATE: Entered STN: 19980625  
 Last Updated on STN: 20000303  
 Entered Medline: 19980612

AB We have used intrinsic fluorescence to test the hypothesis that phosphorylation induces a conformational change in \*\*\*phospholamban\*\*\* (PLB), a regulatory protein in cardiac sarcoplasmic reticulum (SR). Phosphorylation of PLB, which relieves \*\*\*inhibition\*\*\* of the cardiac \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\*, has been shown to decrease the mobility of PLB in sodium dodecyl sulfate-polyacrylamide gel electrophoresis

(SDS-PAGE). In the present study, we found that this mobility shift depends on the acrylamide concentration in the gel, suggesting that phosphorylation increases the effective Stokes radius. To further characterize this structural change, we performed spectroscopic experiments under the conditions of SDS-PAGE. CD indicated that phosphorylation at Ser-16 does not change PLB's secondary structure significantly. However, the fluorescence of Tyr-6 in the cytoplasmic domain of PLB changed significantly upon PLB phosphorylation: phosphorylation increased the fluorescence quantum yield and decreased the quenching efficiency by acrylamide, suggesting a local structural change that decreases the solvent accessibility of Tyr-6. A point mutation (L37A) in the transmembrane domain, which disrupts PLB pentamers and produces monomers in SDS-PAGE and in lipid bilayers, showed similar phosphorylation effects on fluorescence, indicating that subunit interactions within PLB are not crucial for the observed conformational change in SDS. When PLB was reconstituted into dioleoylphosphatidylcholine (DOPC) lipid bilayers, similar phosphorylation effects in fluorescence were observed, suggesting that PLB behaves similarly in response to phosphorylation in both detergent and lipid environments. We conclude that phosphorylation induces a structural change within the PLB protomer that decreases the solvent accessibility of Tyr-6. The similarity of this structural change in monomers and pentamers is consistent with \*\*\*models\*\*\* in which the PLB monomer is sufficient for the phosphorylation-dependent regulation of the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\*.

L12 ANSWER 3 OF 3 BIOSIS COPYRIGHT 2003 BIOLOGICAL ABSTRACTS INC.  
 ACCESSION NUMBER: 2000:95268 BIOSIS  
 DOCUMENT NUMBER: PREV200000095268  
 TITLE: Phospholamban reduces cardiac Ca-ATPase sensitivity to thapsigargin and cyclopiazonic acid.  
 AUTHOR(S): Mahaney, James (1); Barlow, Amy; Honaker, Bob; Huffman, Jamie; Muchnok, Tim  
 CORPORATE SOURCE: (1) Department of Biochemistry, West Virginia University School of Medicine, Morgantown, WV, 26506-9142 USA  
 SOURCE: Archives of Biochemistry and Biophysics, (Dec. 15, 1999) Vol. 372, No. 2, pp. 408-413.  
 ISSN: 0003-9861.  
 DOCUMENT TYPE: Article  
 LANGUAGE: English  
 SUMMARY LANGUAGE: English

AB The \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* of cardiac sarcoplasmic reticulum (CSR) transports Ca<sup>2+</sup> into the CSR to promote muscle relaxation. The \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* is regulated by \*\*\*phospholamban\*\*\*, which \*\*\*inhibits\*\*\* \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* activity by decreasing the apparent affinity of the ATPase for Ca<sup>2+</sup>. \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* \*\*\*inhibition\*\*\* is relieved by phosphorylation of \*\*\*phospholamban\*\*\*, resulting in marked increase in \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* activity (1). Despite considerable progress toward understanding the functional interaction of \*\*\*phospholamban\*\*\* with the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\*, the physical mechanism by which \*\*\*phospholamban\*\*\* reduces the apparent \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* affinity for Ca<sup>2+</sup> is not known. One hypothesis is that \*\*\*phospholamban\*\*\* binds to the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* E2 intermediate state and thereby \*\*\*inhibits\*\*\* the E2-to-E1 conformational transition (2). In this \*\*\*model\*\*\*, \*\*\*phospholamban\*\*\* binding to the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* would increase the steady-state level of the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* in the E2 intermediate at the expense of the E1 intermediate, with a concomitant decrease in the apparent Ca<sup>2+</sup> affinity of the enzyme. To test this hypothesis, we have measured the effect of \*\*\*phospholamban\*\*\* on cardiac \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* \*\*\*inhibition\*\*\* by the specific \*\*\*inhibitors\*\*\* thapsigargin (TG) and cyclopiazonic acid (CPA). TG and CPA are high affinity, specific \*\*\*inhibitors\*\*\* of the SERCA family of ATPases that bind to the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* E2 intermediate and block enzyme turnover by \*\*\*inhibiting\*\*\* the E2-to-E1 cndot Ca<sup>2+</sup> transition (3-5). If \*\*\*phospholamban\*\*\* stabilizes the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* E2 intermediate state, we would expect the \*\*\*Ca\*\*\* - \*\*\*ATPase\*\*\* to be more sensitive to TG and CPA \*\*\*inhibition\*\*\* when \*\*\*phospholamban\*\*\* is regulatory than when \*\*\*phospholamban\*\*\* is uncoupled from the enzyme.



=> d his

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FILE 'MEDLINE, CAPLUS, BIOSIS, EMBASE, SCISEARCH, AGRICOLA' ENTERED AT  
11:04:46 ON 04 MAR 2003

L1 5599 S PHOSPHOLAMBAN  
L2 1495 S L1 (P) (INACTIVAT? OR DEACTIVAT? OR INHIBIT?)  
L3 113184 S (MOLECUL? MODEL?) OR (COMPUTER MODEL?)  
L4 14 S L2 (P) L3  
L5 4 DUPLICATE REMOVE L4 (10 DUPLICATES REMOVED)  
L6 10886 S CYCLIC PEPTIDE  
L7 0 S L2 (P) L6  
L8 5430 S CA-ATPASE  
L9 107 S L8 (P) L2  
L10 19 S L9 (P) MODEL?  
L11 5 DUPLICATE REMOVE L10 (14 DUPLICATES REMOVED)  
L12 3 S L11 NOT L5

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DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS)

SINCE FILE	TOTAL
ENTRY	SESSION
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